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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/746,635	11/13/1996	VADIRAJA MURTHY	96700/341	7843

7590 05/18/2004

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EXAMINER	
GABEL, GAILENE	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 05/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/746,635	MURTHY ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20,24 and 25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20,24 and 25* is/are rejected.

7)☒ Claim(s) *26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/13/04 has been entered.

Amendment Entry

2. Applicant's response filed 2/13/04 is acknowledged. Claims 20 and 24-26 are pending and are under examination.

Rejections Withdrawn

3. In light of Applicant's argument, the rejection of claim 20 under 35 U.S.C. 103(a) as being unpatentable over Olsson et al. (Journal of Applied Biochemistry, 5:437-445 (1983)) is hereby, withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 24 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 24 is vague, indefinite, and confusing in relation to claim 20 from which it depends because claim 20 appears to intend to determine erythrocyte adenylate kinase activity which gives a threshold unit value of "at least about 20 U/L erythrocyte adenylate kinase activity" so as to be indicative of erythrocyte hemolysis, whereas the instant claim recites that the determination of erythrocyte adenylate kinase activity comprises "determining a proportion of erythrocyte adenylate kinase and total adenylate kinase" which reflects a proportion value. Specifically, "20 U/L" is a Unit/Liter unit value and does not reflect a proportion value, i.e. a proportion of 20 U/L erythrocyte adenylate kinase for every 40 U/L total adenylate kinase, or a proportion of 1:2 erythrocyte adenylate kinase to total adenylate kinase, for example. Please clarify.

Claim 25 is indefinite in reciting, "wherein erythrocyte adenylate kinase activity is determined using an antibody that is specific for adenylate kinase" because it implies but does not distinctly and positively define that the antibody specific for adenylate kinase binds adenylate kinase in order to determine erythrocyte adenylate kinase activity.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 20 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olsson et al. (Journal of Applied Biochemistry, 5:437-445 (1983)).

Olsson et al. found that 1) adenylate kinase was concomitantly released with hemoglobin during cell aging, 2) cell aging results in progressive lysis of erythrocytes, 3) adenylate kinase was suitable for monitoring hemolysis due to its extreme storage stability, 4) there was a high degree of correlation between the amount of accumulated hemoglobin and adenylate kinase, 5) and while hemolysis was conventionally measured by measuring extracellular hemoglobin, adenylate kinase activity measurement was also a sensitive and convenient way to follow hemolysis (see page 437, Table 1, and page 445). Olsson et al. determined adenylate kinase activity in plasma by measuring formation of ATP from ADP by firefly luciferase reaction.

Olsson et al. differ from the instant invention in failing to detect hemolysis by determining adenylate kinase activity in serum rather than plasma. However, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of Olsson et al. by determining erythrocyte kinase activity in serum rather than plasma because serum and plasma are conventional alternative samples used in clinical analysis, differing only in the presence or absence of anticoagulation.

6. Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Olsson et al. (Journal of Applied Biochemistry, 5:437-445 (1983)) in view of Matsuura et al. (Journal of Biological Chemistry, 264 (17): 10148-10155 (1989)).

Olsson et al. is discussed supra. Olsson et al. also differ from the instant invention in failing to teach determining erythrocyte adenylate kinase activity using an antibody specific for adenylate kinase.

Matsuura et al. teach that there is an association between adenylate kinase activity (deficiency) in erythrocytes and hemolysis (hemolytic anemia) (see Abstract). Matsuura et al. teach that adenylate kinase (AK1) is present in skeletal muscle, brain, and erythrocyte; thus, adenylate kinase activity has been totally and differentially measured (see page 10148, column 2). Specifically, Matsuura et al. describe immunoblot analysis of human adenylate kinase using antibody (anti AK1 antibody) specific for adenylate kinase (see 10151).

Thus, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to measure adenylate kinase activity in the method of Olsson using

antibody specific for adenylate kinase such as taught by Matsuura because use of antibody in determining the concentration of proteins, antigens, or in this case enzyme, is well known, conventional, and well within ordinary skill.

Response to Arguments

7. Applicant's arguments with respect to claims 20, 24, and 25 have been considered but are moot in view of the new ground of rejection.

A) Applicant argues that the combination of Olsson with Matsuura does not render obvious the claimed invention. Applicant specifically argues that the antibody to adenylate kinase isozyme (AK1) in the method of Matsuura will detect not only erythrocyte adenylate kinase, but also muscle adenylate kinase which may also be present in serum. Thus, the antibody cannot be used to determine solely the level of erythrocyte adenylate kinase in a sample, as required by claim 20.

In response, it is noted that such feature upon which applicant relies, i.e. determine erythrocyte adenylate kinase activity by binding erythrocyte adenylate kinase with an antibody specific thereto, is not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Allowable Subject Matter

8. Claim 26 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Prior art of record does not teach or fairly suggest using an antibody specific for erythrocyte adenylate kinase to bind erythrocyte adenylate kinase, to determine the presence of at least about 20 U/L erythrocyte adenylate kinase activity, and to thus diagnose erythrocyte hemolysis in a subject.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday, Tuesday, and Thursday, 5:30 AM to 2:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-0169.

Gailene R. Gabel
Patent Examiner
Art 1641
May 13, 2004

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641